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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/817,204	04/02/2004	Nagi G. Ayad	10498-00067	3911

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EXAMINER	
LEE, JAE W	

ART UNIT	PAPER NUMBER
1656	

MAIL DATE	DELIVERY MODE
01/22/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/817,204	AYAD ET AL.	
	Examiner	Art Unit	
	JAE W. LEE	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-13,20-22 and 24-55* is/are pending in the application.

4a) Of the above claim(s) *20-22,24,25 and 27-51* is/are withdrawn from consideration.

5)☒ Claim(s) *4,54 and 55* is/are allowed.

6)☒ Claim(s) *1, 3, 5-13, 26, 52 and 53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application Status

In response to the previous Office actions, a non-final rejection (mailed on 04/15/2008), Applicants filed a response and amendment received on 09/15/2008. Said amendment, canceled Claims 2, 14-19 and 23, amended Claims 1, 3 and 7, and added Claims 52-55. Claims 1, 3-13, 26 and 52-55 are at issue and present for examination.

Applicants' arguments filed on 09/15/2008, have been fully considered, and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

It is noted by the Examiner that Claims 20-22, 24, 25 and 27-51 were withdrawn from further consideration by the Examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention, in the previous Office actions, a non-Final rejection (mailed on 12/29/2006).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7 and 54 are rejected under of 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 recites the phrase, “stringent conditions” which is unclear and indefinite. It is noted by the Examiner that “stringent conditions” are not defined in the specification. It is further noted that paragraph [0041] of the specification states that:

> “[a]s used herein, the term "hybridizes under stringent conditions" is intended to describe conditions for hybridization and washing under which nucleotide sequences at least 60% identical to each other *typically* remain hybridized to each other. … A preferred, *non-limiting example* of stringent hybridization conditions are hybridization in 6X sodium chloride/sodium citrate (SSC) at about 45.degree. C., followed by one or more washes in 0.2.times.SSC, 0.1% SDS at 50.degree. C., preferably at 55.degree. C., and more preferably at 60.degree. C. or 65.degree. C.” (italicized for added emphasis).

As such, the recitation of “stringent conditions” is unclear absent a statement of the conditions under which the hybridization reaction is performed. Nucleic acids which will hybridize under some hybridization conditions will not necessarily hybridize under different conditions. The art does not recognize a single set of experimental conditions as “stringent” and the specification does not define what should be regarded as "stringent" as indicated above. While the specification has provided some conditions which are considered “stringent”, these are merely exemplary conditions which do not define all the conditions intended to be "stringent". For examination purposes, it will be assumed that the term “stringent conditions” reads “any hybridization conditions”.

Claim 54 recites the phrase, "The isolated nucleic acid molecule of claim 4 having one or more Tome-1 activities," which is unclear and indefinite. The reason is that Tome-1 activities are properties of the Tome-1 protein, and NOT of the "isolated nucleic acid molecule of claim 4". In the interest of advancing prosecution, the noted phrase is interpreted as "The isolated nucleic acid molecule of claim 4, wherein the said nucleic acid molecule encodes a protein having one or more Tome-1 activities".

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 5-13, 26, 52 and 53 are rejected under 35 U.S.C. § 112, first paragraph, written description, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection was stated in the previous office action as it applied to previous claims 1, 3-13 and 26. In response to this rejection, Applicants have cancelled claim 2, and amended claims 1, 3 and 7, and added claims 52-55, and traverse the rejection as it applies to the newly amended claims.

Applicants point out that the recitation of a nucleotide sequence or amino acid sequence having at least about 85% sequence homology represents a partial structure. That is, at least 85% of the nucleic acids in the sequence will match those of SEQ ID NO:4, SEQ ID NO:5 or SEQ ID NO:6, and at least 85% of the amino acids in the sequence will match those of SEQ ID NO:1, SEQ ID NO:2 or SEQ ID NO:3. The disclosure of SEQ ID NOs:1, 2, 3, 4, 5 and 6 combined with the pre-existing knowledge in the art regarding the genetic code would have put one of skill in the art in possession of the genus of nucleic acids that encode SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6, and the genus of amino acids that encode SEQ ID NO:1, SEQ ID NO:2 and SEQ ID NO:3 (See Written Description Training Materials, Revision 1, March 25, 2008, pages 37 and 38). Thus, the instant specification provides adequate written description for claims 52 and 53. Amended claims 1 and 3 and claims depending therefrom recite an amino acid sequence or nucleic acid molecule, respectively, having 80% sequence homology to SEQ ID NO:1, SEQ ID NO:2 or SEQ ID NO:3 (claim 1) or 80% sequence homology to SEQ ID NO:4, SEQ ID NO:5 or SEQ ID NO:6 (claim 3). Claims 5 and 6 and claims depending therefrom recite nucleic acid molecule or amino acid sequence, respectively, having 85% sequence homology to SEQ ID NO:4, SEQ ID NO:5 or SEQ ID NO:6 (claim 5) or 80% sequence homology to SEQ ID NO: 1, SEQ ID NO:2 or SEQ ID NO:3 (claim 6).

Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. First, claims are drawn to a genus of isolated nucleic acid molecules from a eukaryotic cell, [1] wherein said nucleic acid molecules

comprises any nucleic acid sequence with at least about 80% or 85% sequence homology to a nucleic acid comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6, or [2] which encodes a polypeptide comprising any amino acid sequence having at least about 80% or 85% sequence homology to an amino acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO:2 and SEQ ID NO:3, wherein the polypeptide has one or more trigger of mitotic entry 1 (Tome-1) activities; wherein said activities are selected from the group consisting of: a) modulating ubiquitinylation of wee1 protein; b) modulating degradation of wee1 protein; c) modulating Skp-Cullin-F-box protein complex (SCF complex) components, wherein said components are Skp-1, Cul-1, Rbx and an F Box substrate; d) modulating entry of a cell into the cell cycle; e) modulating progression of a cell through the cell cycle; f) modulating release of a cell from the cell cycle; g) modulating cell growth; h) modulating cellular proliferation; i) modulating tumorigenesis; and j) modulating mitogenesis. In other words, the recited genus of isolated nucleic acid sequences encompasses any polynucleotide sequences [1] having at least 80% or 85% sequence homology to SEQ ID NOs: 4-6, or [2] which encodes any amino acid sequence having at least 80% or 85% sequence homology to SEQ ID NOs: 1-3, as long as the encoded protein has the broadly defined functions or activities as recited in a) through j). Such a broad genus of isolated nucleic acid molecules with widely variant structures, wherein the proteins encoded by said nucleic acid molecules have many different broadly defined functions/activities as recited in a) through j) are not adequately described by the disclosure of the specification because

said disclosure is limited to polynucleotides having the nucleotide sequences of SEQ ID NOs: 4-6 which encode the mouse, human and Xenopus Tome-1 proteins as set forth in SEQ ID NOs: 1-3, respectively, wherein said Tome-1 proteins interact with phosphorylated Wee1 for ubiquitination-dependent Wee-1 degradation. The reason is that a complex network of proteins having widely variant biological activities, i.e., widely variant activities of cell-cycle check point proteins at [1] G0, [2] G1, [3] S, [4] intra S, [5] G2 and [6] M just to mention a few, are required for modulating entry of a cell into the cell cycle. As such, widely variant functions/activities described in d)-j) of claim 1, are not described by the specification. Furthermore, widely variant nucleic acid sequences encoding proteins having mere 80% or 85% sequence homology to SEQ ID NOs 1-3 with widely variant functions, i.e., especially those activities recited in d) through j) in claim 1, are not adequately described by the specification. It is well-known and accepted in the relevant art that proteins having very similar structure can have different activities. See Witkowski et al., (Biochemistry, 38, 11643-11650, 1999), and Wishart et al., (Journal of Biological Chemistry, Vol. 270, No. 45, pp. 26782–26785, 1995). In light of this notion, one of skill in the art would not have recognized that Applicants were in possession of any isolated nucleic acid molecule [1] having at least 80% or 85% sequence homology to SEQ ID NOs: 4-6, or [2] which encodes any amino acid sequence having at least 80% or 85% sequence homology to SEQ ID NOs: 1-3, in addition to having widely variant functions as described in d)-j) of claim 1.

Newly added claims 52 and 53 are rejected under this statute for the same reasons provided herein and in the previous office actions.

Please refer to the M.P.E.P. section 2163 [R-5] under II, A, 3, (a), (ii) for more details with respect to sufficient number of representative species that should be disclosed to describe a widely variant genus.

Given the lack of additional representatives of a genus of isolated nucleic acid molecules [1] having at least 80% or 85% sequence homology to SEQ ID NOs: 4-6, or [2] which encodes any amino acid sequence having at least 80% or 85% sequence homology to SEQ ID NOs: 1-3, in addition to having widely variant functions, as encompassed by the claim, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1, 3, 5-13, 26, 52 and 53 are rejected under 35 U.S.C. 112, first paragraph, scope of enablement, because the specification, while being enabling for isolated nucleic acid molecules comprising the nucleotide sequences of SEQ ID NOs: 4-6 which encode the mouse, human and Xenopus Tome-1 proteins as set forth in SEQ ID NOs: 1-3, respectively, wherein said Tome-1 proteins interact with phosphorylated Wee1 for ubiquitination-dependent Wee-1 degradation, does not reasonably provide enablement for any isolated nucleic acid molecule [1] having at least 80% or 85% sequence homology to SEQ ID NOs: 4-6, or [2] which encodes any amino acid

sequence having at least 80% or 85% sequence homology to SEQ ID NOs: 1-3, in addition to having widely variant functions as described in a)-j) of claim 1. Therefore, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The rejection was stated in the previous office action as it applied to previous claims 1, 3-13 and 26. In response to this rejection, Applicants have cancelled claim 2, amended claims 1, 3 and 7, and added claims 52-55, and traverse the rejection as it applies to the newly amended claims.

Applicants respectfully submit that the instant specification provides ample direction and guidance to make and use an isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6 as well as to make and use an isolated nucleotide sequence containing 80% or 85% sequence homology to SEQ ID NO:4, SEQ ID NO:5 or SEQ ID NO:6. Applicants respectfully submit that the instant specification provides ample direction and guidance to make and use an amino acid sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO:2 and SEQ ID NO:3 as well as to make and use an amino acid sequence containing 80% or 85% sequence homology to SEQ ID NO:1, SEQ ID NO:2 or SEQ ID NO:3. Applicants provide the nucleotide sequence for each of SEQ ID NO:4, SEQ ID NO:5 and SEQ ID NO:6, and provide the amino acid sequences for each of SEQ ID NO: 1, SEQ ID NO:2 and SEQ ID NO:3. In view of the sequence information that Applicants provide and in view of the knowledge and skill of

one of ordinary skill in the art at the time of filing, determining whether a nucleic acid molecule includes a sequence set forth as SEQ ID NO:4, SEQ ID NO:5 or SEQ ID NO:6 or a sequence having 80% or 85% sequence homology thereto would involve only routine screening using techniques that were well known in the art at the time of filing. Similarly, determining whether an amino acid sequence includes a sequence set forth as SEQ ID NO:1, SEQ ID NO:2 or SEQ ID NO:3 or a sequence having 80% or 85% sequence homology thereto would involve only routine screening using techniques that were well known in the art at the time of filing.

Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. First, Claims are so broad to encompass any isolated nucleic acid molecule [1] having at least 80% of 85% sequence homology to SEQ ID NOs: 4-6, or [2] which encodes any amino acid sequence having at least 80% or 85% sequence homology to SEQ ID NOs: 1-3, in addition to having widely variant functions as described in a)-j) of claim 1. The specification, however, does not support the broad scope of the claims which encompass all modifications and fragments of any isolated nucleic acid molecule [1] having at least 80% or 85% sequence homology to SEQ ID NOs: 4-6, or [2] which encodes any amino acid sequence having at least 80% or 85% sequence homology to SEQ ID NOs: 1-3, as long as it has widely variant functions as described in a)-j) of claim 1. For instance, the specification does not provide support for making and using an isolated nucleic acid molecule having 80% or 85% sequence homology to SEQ ID NO: 4, which *increases* tumorigenesis while *decreasing* cellular proliferation. Furthermore, the specification does not enable one of

skill in the art how to make and use an isolated nucleic acid molecule having 80% sequence homology to SEQ ID NO: 4 which *increases only* the cellular proliferation without affecting the tumorigenesis, or vise versa, all of which are encompassed by the claimed language, "one or more Tome-1 activities; wherein said activities are selected from the group consisting of: … modulating cell growth [or cellular proliferation, tumorigenesis, mitogenesis, etc]." Given the widely variant biological activities that encompassed by the activities recited in d) through j) of claim 1 as explained above, in addition to the notion that proteins having very similar structure can have different activities (see Witkowski et al., and Wishart et al.), it would be undue experimentation for one of skill in the art to make and use the claimed invention.

Newly added claims 52 and 53 are rejected under this statute for the same reasons provided herein and in the previous office actions.

Taken together, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any isolated nucleic acid molecule [1] having at least 80% or 85% sequence homology to SEQ ID NOs: 4-6, or [2] which encodes any amino acid sequence having at least 80% or 85% sequence homology to SEQ ID NOs: 1-3, in addition to having widely variant functions as described in a)-j) of claim 1 having the desired biological characteristics is unpredictable and the experimentation left to those

skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

Claims 1, 3, 5-13, 26 and 53 are rejected under 35 U.S.C. 102(b) as anticipated by Walker et al. (WO/2002/018575).

The rejection was stated in the previous office action as it applied to previous claims 1-3, 5-13 and 26. In response to this rejection, Applicants have cancelled claim 2, amended claims 1, 3 and 7, and added claims 52-55, and traverse the rejection as it applies to the newly amended claims.

Applicants argue that Walker et al. do not teach that SEQ ID NO: 3 encodes any polypeptide, Let alone a polypeptide having at least 80% homology to SEQ ID NO: 2. and/or one or more Tome-1 activities.

Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons. First, it is noted that there are no new issues, which are raised in the instant rejection. For Applicants convenience and clarity, the instant rejection of record is outlined herein with minor modifications to account for Applicants' new amendment to claims.

Walker et al. teach genes expressed in the cell cycle. Walker et al. specifically teach an isolated nucleic acid molecule (SEQ ID NO:3 of WO/2002/018575), which has 97% sequence homology to the Applicant's SEQ ID NO: 5, wherein the SEQ ID NO:3 of WO/2002/018575 encodes an amino acid sequence having at least 85% sequence

homology to Applicant's SEQ ID NO: 2, wherein the SEQ ID NO:3 of WO/2002/018575 has one or more Tome-1 activities (see the sequence alignment result below). It is noted that because Walker et al.'s SEQ ID NO: 3 and Applicants' SEQ ID NO: 5 are nearly identical, i.e., having 97% sequence homology, it is an inherent property of Walker et al.'s SEQ ID NO: 3 to encode a polypeptide having at least 85% sequence homology to Applicant's SEQ ID NO: 2, and the encoded polypeptide would inherently possess one or more Tome-1 activities as recited in claims.

Teachings of Walker et al. also anticipate the limitations of Claims 7, 8 and 26 because it is an inherent property of SEQ ID NO:3 of WO/2002/018575, which is 97% homologous to the Applicant's SEQ ID NO: 5, to hybridize to and be complementary to the Applicant's SEQ ID NO: 5 under any hybridization conditions (see above 112 2nd paragraph rejection). Walker et al. further teach the hybridization conditions and methods using the cDNAs of the Sequence Listing as disclosed on pg. 24-27 under section heading "VIII Hybridization Technologies and Analyses. Walker et al. also teach complementary molecules to the cDNA for use in detection and inhibition of gene expression on pg. 27-28 under section heading "IX Complementary Molecules."

Walker et al. teach the protein expression of the cDNA in their Sequence Listing using pUB6/V5-His vector in either CHO cells for mammalian expression or Sf9 cells for insect cell expression (see pg. 28 under section heading "Protein Expression). The expressed proteins cloned in pUB6/V5-His expression vectors comprise affinity tags consisting of V5 epitope and His_6, making the expressed proteins a heterologous protein. Therefore, Walker et al. anticipate Claims 9-13.

The newly added claim 53 is included in this rejection for the same reasons provided herein and in the previous office actions.

It is noted that “Qy” refers to Applicants’ SEQ ID NO: 5, and “Db” refers to SEQ ID NO: 3 in Walker et al.

```
RESULT 7
AX458895
LOCUS       AX458895               1324 bp    DNA     linear   PAT 08-JUL-2002
DEFINITION  Sequence 3 from Patent WO0218575.
ACCESSION   AX458895
VERSION     AX458895.1  GI:21725489
KEYWORDS    .
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  ORGANISM  Homo sapiens
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            Mammalia; Eutheria; Euarchontoglires; Primates; Catarrhini;
            Hominidae; Homo.
REFERENCE   1
  AUTHORS   Walker,M.G. and Jung,K.
  TITLE     Genes expressed in the cell cycle
  JOURNAL   Patent: WO 0218575-A 3 07-MAR-2002;
            Incyte Genomics, Inc. (US)
FEATURES             Location/Qualifiers
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ORIGIN

  Query Match             97.2%;  Score 1107;  DB 2;  Length 1324;
  Best Local Similarity   99.9%;  Pred. No. 0;
  Matches 1118;  Conservative    0;  Mismatches    0;  Indels    1;  Gaps    1;

Qy          1 CCACGAGCTGTTGTGCATCCAGAGGTGGAATTGGGGCCCGGCATTCCCTCCTCGTCCCGG 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        206 CCACGAGCTGTTGTGCATCCAGAGGTGGAATTGGGGCCCGGCATTCCCTCCTCGTCCCGG 265

Qy         61 GCTGGCCCTTG-CCCCCACCCTGCAACTCCTGGTTGAGATGGGCTCAGCCAAGAGCGTCC 119
              |||||||||||| ||||||||||||||||||||||||||||||||||||||||||||||
Db        266 GCTGGCCCTTGCCCCCCACCCTGCAACTCCTGGTTGAGATGGGCTCAGCCAAGAGCGTCC 325

Qy        120 CAGTCACACCAGCGCGGCCTCCGCCGCACAACAAGCATCTGGCTCGAGTGGCGGACCCCC 179
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Qy        180 GTTCACCTAGTGCTGGCATCCTGCGCACTCCCATCCAGGTGGAGAGCTCTCCACAGCCAG 239
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Qy        240 GCCTACCAGCAGGGGAGCAACTGGAGGGTCTTAAACATGCCCAGGACTCAGATCCCCGCT 299
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Qy        300 CTCCTACTCTTGGTATTGCACGGACACCTATGAAGACCAGCAGTGGAGACCCCCCAAGCC 359
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        506 CTCCTACTCTTGGTATTGCACGGACACCTATGAAGACCAGCAGTGGAGACCCCCCAAGCC 565
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Qy        360 CACTGGTGAAACAGCTGAGTGAAGTATTTGAAACTGAAGACTCTAAATCAAATCTTCCCC 419
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Qy        420 CAGAGCCTGTTCTGCCCCCAGAGGCACCTTTATCTTCTGAATTGGACTTGCCTCTGGGTA 479
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Qy        540 AGGTGTTTTCCAAGGAGGAAGCAAGACAGCCCACAGAAACCCCTGTGGCCAGCCAGAGCT 599
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
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Qy        600 CCGACAAGCCCTCAAGGGACCCTGAGACTCCCAGATCTTCAGGTTCTATGCGCAATAGAT 659
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        806 CCGACAAGCCCTCAAGGGACCCTGAGACTCCCAGATCTTCAGGTTCTATGCGCAATAGAT 865

Qy        660 GGAAACCAAACAGCAGCAAGGTACTAGGGAGATCCCCCCTCACCATCCTGCAGGATGACA 719
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db        866 GGAAACCAAACAGCAGCAAGGTACTAGGGAGATCCCCCCTCACCATCCTGCAGGATGACA 925

Qy        720 ACTCCCCTGGCACCCTGACACTACGACAGGGTAAGCGGCCTTCACCCCTAAGTGAAAATG 779
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Db        926 ACTCCCCTGGCACCCTGACACTACGACAGGGTAAGCGGCCTTCACCCCTAAGTGAAAATG 985

Qy        780 TTAGTGAACTAAAGGAAGGAGCCATTCTTGGAACTGGACGACTTCTGAAAACTGGAGGAC 839
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Qy        840 GAGCATGGGAGCAAGGCCAGGACCATGACAAGGAAAATCAGCACTTTCCCTTGGTGGAGA 899
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Qy        900 GCTAGGCCCTGCATGGCCCCAGCAATGCAGTCACCCAGGGCCTGGTGATATCTGTGTCCT 959
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1106 GCTAGGCCCTGCATGGCCCCAGCAATGCAGTCACCCAGGGCCTGGTGATATCTGTGTCCT 1165

Qy        960 CTCACCCCTTCTTTCCCAGGGATACTGAGGAATGGCTTGTTTTCTTAGACTCCTCCTCAG 1019
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1166 CTCACCCCTTCTTTCCCAGGGATACTGAGGAATGGCTTGTTTTCTTAGACTCCTCCTCAG 1225

Qy       1020 CTACCAAACTGGGACTCACAGCTTTATTGGGCTTTCTTTGTGTCTTGTGTGTTTCTTTTA 1079
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1226 CTACCAAACTGGGACTCACAGCTTTATTGGGCTTTCTTTGTGTCTTGTGTGTTTCTTTTA 1285

Qy       1080 TATTAAAGGAAGTAATTTTAAATGTTACTTTAAAAAGGT 1118
              |||||||||||||||||||||||||||||||||||||||
Db       1286 TATTAAAGGAAGTAATTTTAAATGTTACTTTAAAAAGGT 1324
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Therefore, Walker et al. anticipate claims 1, 3, 5-13, 26 and 53.

The examiner has presented evidence to reasonably support the polynucleotide of the prior art, which is encompassed by the claim. According to MPEP 2112.V, once a reference teaching a product appearing to be substantially identical is made the basis of

a rejection, and the examiner presents evidence or reasoning tending to show inherency, the burden shifts to the applicant to show an unobvious difference.

Since the Office does not have the facilities for examining and comparing applicants' polynucleotide (or the encoded protein) with the polynucleotide (or the encoded protein) of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed product and the product of the prior art (i.e., that the polynucleotide of the prior art does not possess the same material structural and functional characteristics of the claimed polynucleotide). See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzgerald* et al., 205 USPQ 594.

For the reasons provided herein and in the previous office actions, the rejection under this statute is maintained.

The previous rejection of Claims 1, 3, 5-8, 10 and 26 under 35 U.S.C. 102(b) as anticipated by Zhao et al. (Human *CDC23:* cDNA Cloning, Mapping to 5q31, Genomic Structure, and Evaluation as a Candidate Tumor Suppressor Gene in Myeloid Leukemias, GENOMICS 53, 184–190, 1998) as evidenced by Walker et al. (WO/2002/018575), is withdrawn because CDC23 is different from SEQ ID NO: 3 of Walker et al.

Conclusion

Claims 1, 3, 5-13, 26, 52 and 53 are rejected for the reasons identified in this Office action. Claims 4, 54 and 55 are allowable over the prior art of record. Applicants

must respond to the objections/rejections in each section in this Office action to be fully responsive in prosecution.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jae W. Lee whose telephone number is 571-272-9949. The examiner can normally be reached on M-F between 9:30-7.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on 571-272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

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/JAE W LEE/
Examiner, Art Unit 1656

/Rebecca E. Prouty/
Primary Examiner,
Art Unit 1652